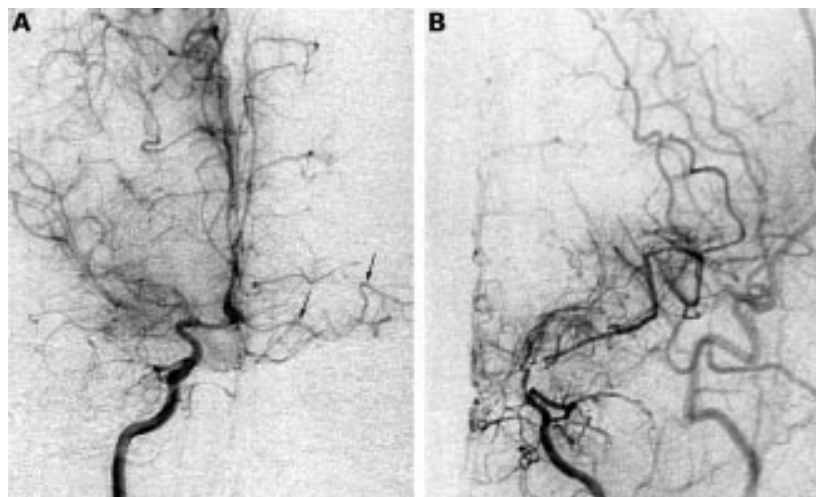


## LETTERS TO THE EDITOR

### Accessory middle cerebral artery and moyamoya disease

A rare association of moyamoya disease with the accessory middle cerebral artery was seen in two patients. The terminal portions of bilateral internal carotid arteries and their vicinities were markedly stenotic and so-called moyamoya vessels developed at the base of the brain. The left accessory middle cerebral artery originating near the anterior communicating artery supplied the left anterior frontal lobe in both patients. Although the accessory middle cerebral artery coursed in the vicinity of the markedly stenotic terminal portion of the left internal carotid artery, the artery was not stenotic. This finding implies that the steno-occlusive changes in the cerebral vasculature in moyamoya disease have topological predilection to the distal internal carotid arteries.

Moyamoya disease is characterised by angiographic features of steno-occlusive changes of the terminal portions of bilateral intracranial internal carotid arteries as well as dilated perforating arteries at the base of the brain known as "moyamoya" vessels. The clinical manifestation of moyamoya disease is typically brain ischaemia in the paediatric population and brain haemorrhage in adults.<sup>1</sup> The accessory middle cerebral artery is a variation of middle cerebral artery branching



**Figure 2** (A) Right carotid angiography (anterior-posterior view) shows stenotic change at the origin of the right middle cerebral artery, but the right anterior cerebral artery is normal. The left accessory middle cerebral artery (arrows) originates near the anterior communicating artery coursing parallel to the left middle cerebral artery. (B) Left carotid angiography (anterior-posterior view) shows severe steno-occlusive changes at the terminal portion of the internal carotid artery with development of moyamoya vessels.

and its incidence has been reported to be 0.3–4.0%.<sup>2-4</sup> The accessory middle cerebral artery originates from either the proximal or distal horizontal portion of the anterior cerebral artery coursing parallel to the horizontal portion of the middle cerebral artery and reaches the anterior frontal lobe.<sup>5</sup>

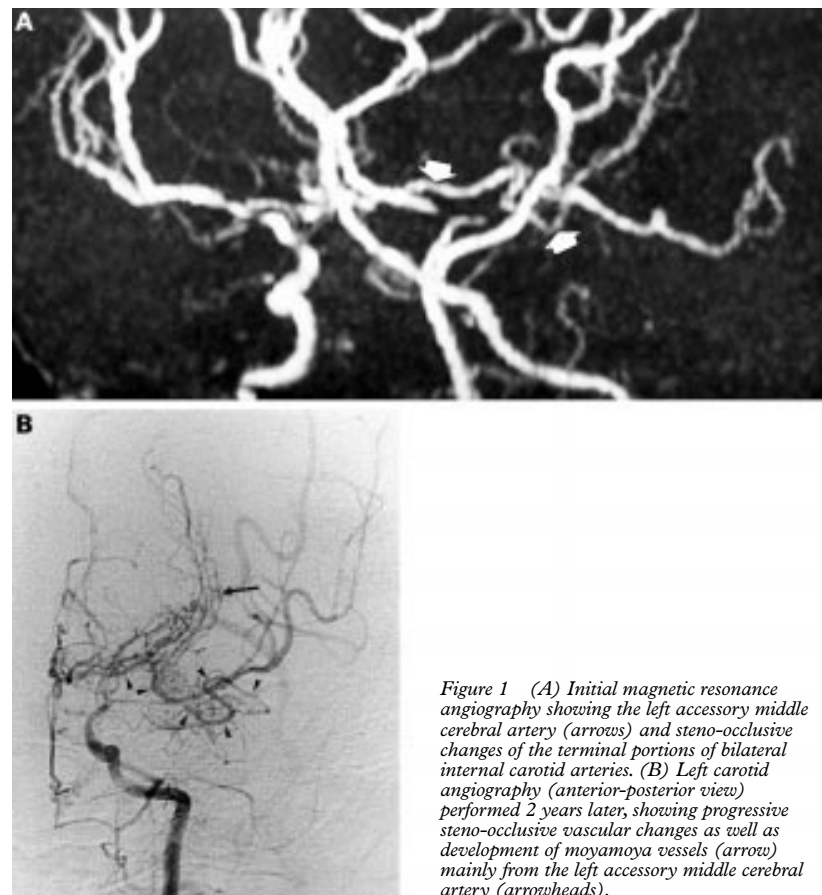
Patient 1, a 32 year old woman, had presented with a transient ischaemic attack of right hemiparesis 2 years before the current episode. Results of initial MRI imaging performed at another hospital were inter-

preted as normal, but MR angiography showed steno-occlusive changes of the terminal portions of bilateral intracranial internal carotid arteries. Stenotic changes were more severe on the left than on the right side. Although the proximal portion of the left middle cerebral artery was markedly stenotic on MR angiography, the left accessory middle cerebral artery was clearly shown to be without stenosis (fig 1 A). The patient was treated conservatively.

No recurrent ischaemic attack had occurred over a period of 2 years until the patient began to experience transient ischaemic attacks of right hemiparesis several times a month. She was referred to us for further evaluation. She was neurologically normal and history was not contributory except for mild hypertension for 2 years. Digital subtraction angiography showed progressive steno-occlusive changes of the terminal portions of the internal carotid arteries as well as development of moyamoya vessels, which were consistent with the diagnosis of moyamoya disease (fig 1 B). Most moyamoya vessels on the left side originated from the accessory middle cerebral artery. This patient subsequently underwent bypass surgery bilaterally. Frequency of transient ischaemic attacks reduced markedly during the follow up period of 3 months postoperatively.

Patient 2 was a 30 year old man admitted for re-evaluation of moyamoya disease. This patient experienced occasional headache and vomiting at the age of 5 years. At the age of 11 years, transient ischaemic attacks of right hemiparesis developed to a rate of one a week. The diagnosis of moyamoya disease was established by cerebral angiography. He underwent bilateral bypass surgery subsequently at the age of 13 years in another hospital. He had experienced no ischaemic episodes for 17 years thereafter and he thought that moyamoya disease was cured. He came to our hospital when he had minor head trauma at the age of 30 years and was advised to re-evaluate the disease.

At admission, the patient was neurologically normal. Brain MRI showed no parenchymal abnormality. Single photon emission computed tomography was normal. Right carotid angiography showed severe stenotic



**Figure 1** (A) Initial magnetic resonance angiography showing the left accessory middle cerebral artery (arrows) and steno-occlusive changes of the terminal portions of bilateral internal carotid arteries. (B) Left carotid angiography (anterior-posterior view) performed 2 years later, showing progressive steno-occlusive vascular changes as well as development of moyamoya vessels (arrow) mainly from the left accessory middle cerebral artery (arrowheads).

change of the proximal right middle cerebral artery, but the right anterior cerebral artery was normal. The left accessory middle cerebral artery originated near the anterior communicating artery (fig 2 A). Left carotid angiography showed severe stenosis at the terminal portion of the internal carotid artery with moderate development of moyamoya vessels (fig 2 B). The left accessory middle cerebral artery was not stenotic despite the vicinity of the markedly stenotic distal internal carotid artery and middle cerebral artery. Moyamoya vessels were not supplied by the left accessory middle cerebral artery. The patient was conservatively followed up for 6 months without any ischaemic episodes.

An association of the accessory middle cerebral artery and cerebral aneurysms has been well documented.<sup>2,6</sup> Moyamoya disease is highly associated with primitive carotid-basilar anastomosis, such as with the primitive trigeminal arteries and their variants.<sup>7</sup> To our knowledge, however, an association of the accessory middle cerebral artery with moyamoya disease has not been reported. The accessory middle cerebral artery was first regarded as a hypertrophied recurrent artery of Heubner.<sup>8</sup> However, it is now thought to be a cortical branch of the middle cerebral artery supplying the anterior frontal lobe, which is annexed to the embryological early artery, the anterior cerebral artery.<sup>5</sup> The accessory middle cerebral artery can serve as a collateral blood supply when the internal carotid artery or middle cerebral artery, or both are stenotic or occluded,<sup>9</sup> as was the case in our patients.

Our patients are interesting in that (a) the accessory middle cerebral artery was associated with moyamoya disease and (b) the accessory middle cerebral artery was not stenotic even though the distal internal carotid artery and the proximal middle cerebral artery showed steno-occlusive changes. Stenotic changes were not seen in the accessory middle cerebral artery although it coursed in the vicinity of the stenotic horizontal portion of the middle cerebral artery. This implies that susceptibility to arterial stenotic change is limited to the distal portion of the internal carotid artery and the proximal middle cerebral artery but not to the accessory artery even though all of these vessels are in close proximity. The cause of moyamoya disease is still unknown, but we think that there is a topographic difference in the predilection to stenotic changes in the cerebral vasculature in the disease.

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### Maternal age is not a risk factor for Parkinson's disease

The aging process is associated with an accumulation of oxidative damage to mitochondrial DNA (mtDNA).<sup>1,2</sup> Mutations and deletions of mtDNA accumulate with aging in various tissues including germ lines.<sup>3,4</sup> The resulting mitochondrial defects, if transmitted to offspring through the maternal line, could potentially play a part in the pathogenesis of several neurodegenerative illnesses including Parkinson's disease.<sup>5</sup> In addition, advanced maternal age at the time of conception results in increased risk of genetic birth defects. This is in part due to chromosomal mutations and malfunctions within the ova which are in turn due to the increased age of the ovary and the ova. We examined the age of mothers at birth of patients with Parkinson's disease and controls to evaluate whether maternal age may be a risk factor in the development of Parkinson's disease.

Subjects were recruited from the Movement Disorders Clinic at the University of Virginia. We interviewed 629 consecutive patients with Parkinson's disease and 376 consecutive spousal controls regarding their mother's age at the time of the subject's birth (maternal age). The diagnosis of Parkinson's disease was based on internationally accepted criteria. At least two of the following three criteria had to be present: rest tremor, cogwheel rigidity, and bradykinesia. Asymmetry of these features at the time of diagnosis and at onset had to be present. Exclusion criteria included presence of atypical features, presence of a pre-existing possible cause, definite absence of response to levodopa, and a clearly non-progressive course over at least 3 years. Moreover, 69% of the patients with Parkinson's disease had been examined on multiple occasions thus increasing both our confidence in and accuracy of the diagnosis of Parkinson's disease.

The original data set of 1005 subjects was reduced to obtain groups of equal size as well as groups similar in sex proportion and age. Firstly, we excluded 79 cases in which maternal age was missing. This elimination of cases with missing data resulted in the groups being of similar age. From the new data set of 926 informants, we next randomly selected men and women from each subject group. The number of subjects to be selected was determined by the minimum group, the male control group (n=106), for which we were able to ascertain maternal age and also preserve the 1.5:1 male to female sex ratio found in the original sample. After this final exclusion of 572 cases, complete data from 177 patients with Parkinson's disease and 177 control subjects were used for the data analyses.

Data were analyzed using Student's *t* test for continuous variables and  $\chi^2$  tests for categorical variables. Logistic regression was performed to determine whether maternal

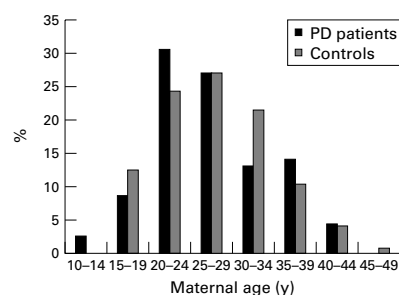


Figure 1 Proportion of subjects by maternal age.

age was associated with risk of Parkinson's disease. All probability (p) values are two tailed.

The Parkinson's disease group and the control group each comprised 106 men (60%) and 71 women. The mean age (SD) of the patients was 67 (10) years compared with the control group mean age (SD) of 66 (10) (p=0.41). The age of onset of symptoms of Parkinson's disease among the patient group ranged from 32-82 years with a mean (SD) of 59 (11) years. Sixty three per cent of the patients received their diagnosis within 2 years of symptom onset (range <1 year to 10 years, with a mean (SD) of 1 year (1.8)).

The age of mothers at the time of the patients' birth ranged from 13 to 43 years with a mean (SD) of 27 (7) years. In the control group, maternal age ranged from 15-49 years with a mean (SD) of 27 (7) years. There was no difference between the groups for mean maternal age (p=0.63).

Maternal age was recoded into eight groups of 5 year increments. The percentage of patients and controls in each maternal age group is shown in figure 1. Not surprisingly, the greatest number of patients and controls were born to women age 20 to 35 years. Analysis by  $\chi^2$  showed no significant differences in the proportion of patients and controls across the maternal age categories (p=0.09).

Logistic regression examined the association between maternal age and Parkinson's disease. The odds ratio (0.99) for maternal age was not significant (p=0.63; 95% confidence interval (95% CI) 0.96-1.02) indicating that maternal age did not influence the risk of developing Parkinson's disease.

Our data show no differences between patients and controls for the age of mothers at the time of the subjects' birth. In fact, the distribution curve of mothers' age at the time of birth of patients with Parkinson's disease closely approximated the maternal birth curve of the control group. In addition, we found no differences in the proportion of patients and controls when maternal age was grouped in 5 year increments. Although a greater number of patients were born to women between ages 35 and 44, and only control group subjects were born to women over 44 years of age, these differences were not significant. Furthermore, the odds ratio did not approach significance, indicating that maternal age also did not affect the risk of developing Parkinson's disease.

The results of this study suggest that genetic mutations acquired by aging oocytes are not pivotal in the development of Parkinson's disease. If acquired mtDNA mutations of female gametes were a significant factor in the pathogenesis of Parkinson's disease, maternal age at birth would be higher for patients with Parkinson's disease than for age

matched controls. These data show no difference in maternal age at birth between patients and controls. Thus, transmission to offspring of somatic mtDNA mutations that accumulate as the mothers age is unlikely to play a part in the cause of Parkinson's disease. However, the results of this study do not exclude a role for inherited abnormalities of mtDNA mutations in this disease. Homoplasmic polymorphisms or heteroplasmic sequence abnormalities could still account for a proportion of those with Parkinson's disease. Indeed, either of these possibilities, especially heteroplasmy, is consistent with the high degree of variability in the clinical expression of mtDNA mutations and the apparent sporadic occurrence of this disease.

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### Hippocampal involvement in identical twins with neurofibromatosis type 1

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder due to a defect on the long arm of chromosome 17. Since 1986, when Cohen *et al*<sup>1</sup> first drew attention to changes on MRI in NF1, it has increasingly been recognised that up to 75% of children with NF1 have lesions, seen most often in the brain stem, cerebellum, optic tracts, and basal ganglia.<sup>2</sup> They are asymptomatic, usually less prominent with age, and the limited available postmortem data suggest that they involve areas of spongiotic or vacuolar change.<sup>3</sup> It is unclear how often temporal lobe structures are involved and figures range from 0% to 16%.<sup>4,5</sup> We report on a pair of identical twins with NF1, with prominent bilateral changes in hippocampal MRI, one of whom presented with a major amnesic syndrome.

The twins, aged 15, were the only children of non-consanguineous unaffected parents with no known family history. Twin 1 had been considered bright throughout his schooling, until in summer 1999 he was involved in a relatively minor fight when another boy punched him a few times and the two boys fell onto a grass lawn without losing consciousness or otherwise sustaining serious head injuries. Five days later his mother became aware of him having memory difficulties; he twice forgot to take a letter to school and then came home recollecting nothing of an evening spent at a church youth group. On admission to hospital he was noted to have greater than 15 café au lait spots and axillary freckling. Visual acuities were normal and there were no major focal neurological

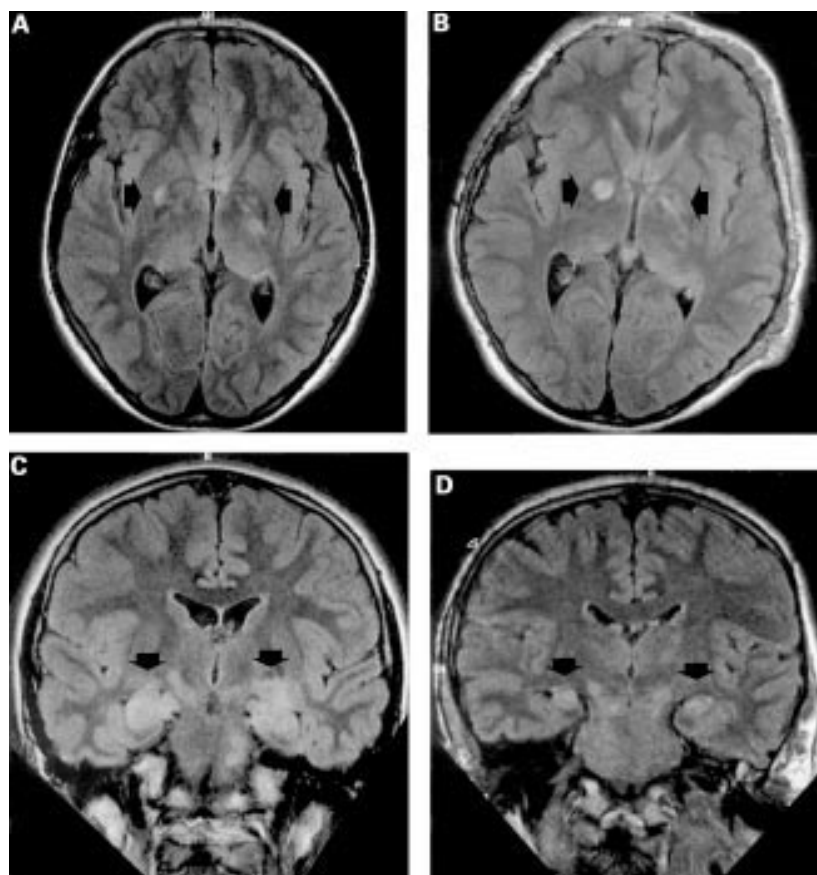


Figure 1 (A) and (B) show flare sequence axial MRI of twin 1 and twin 2 respectively demonstrating virtually identical lesions in the region of both internal capsules highlighted with arrowheads. (C) and (D) show flare sequence coronal MRI scans of twin 1 and twin 2 respectively through the temporal lobe regions showing high signal changes in the hippocampi bilaterally (highlighted with arrowheads) more marked in twin 1 than twin 2.

findings. Because of the acute memory problems herpes simplex encephalitis was considered despite a normal EEG and CSF examination and he was given acyclovir, without benefit. His brain MRI showed multiple areas of increased signal in the medulla, pons, midbrain, and internal capsule regions (fig 1 A), prominent bilateral lesions in the hippocampus, amygdala, and medial temporal cortex (fig 1 C), and enlargement of the optic chiasm with increased signal strongly suggestive of an optic nerve glioma. Extensive blood tests including treponemal serology and chest radiographs were normal. Psychometric testing confirmed twin 1 to have an IQ in the high average range but to have a dense generalised anterograde amnesia. He was able to recall a story immediately it was told but at 5 minutes could only recollect one out of 20 details. Similarly, his immediate copy of the Rey-Osterrieth complex figure was normal (32/36) but he had almost no recall of the figure at 30 minutes (1/2 out of 36). Repeat MRI and neuropsychological assessment 1 year later showed no significant changes.

Because of the lack of a clear diagnosis on twin 1 we also studied his identical twin brother. Southern blot analysis confirmed their monozygosity. Aged 2, twin 2 developed a right facial plexiform neurofibroma and aged 8 a plexiform neurofibroma involving his tongue and larynx was surgically excised. He also had typical cutaneous lesions. His brain MRI showed remarkably similar changes to those seen in twin 1 in the medulla, pons, midbrain, internal capsule (fig 1 B), and hippocampal regions (fig 1 D)

although the changes were less marked in the limbic regions in twin 2 than twin 1. The sole major difference was the normal optic chiasm in twin 2. Neuropsychometry on twin 2 disclosed a full scale IQ in the average range with no evidence of significant amnesic problems.

There are three main areas of interest that arise from these twins. The first is how remarkably similar are the changes on brain MRI. The second is that unlike previous studies<sup>6-8</sup> they are discordant for optic nerve gliomas. The third, and perhaps most intriguing, is twin 1's amnesiac syndrome, the cause of which remains unestablished. He does not seem to have any of the conditions known to cause profound amnesia with changes on MRI, which include herpes simplex encephalitis, paraneoplastic limbic encephalitis, and possibly neurosyphilis.<sup>9</sup> As he has NF1 associated with bilateral hippocampal changes on MRI it is tempting to speculate that the combination of the minor head injury and the lesions in the limbic cortex are responsible. Less likely explanations are malignant gliomatous transformation of hippocampal hamartoma or spread of malignant tissue from his optic nerve glioma.

Changes in MRI specifically within the hippocampus have apparently not been the subject of detailed analysis in NF1 and this paper suggests the need for further study of hippocampal structure and function in NF1.

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### Paroxysmal hypertension during a complex partial seizure

The autonomic mechanisms involved in neurogenic paroxysmal hypertension are not understood. We present the first demonstration of the precise haemodynamic and autonomic changes during a complex partial seizure.

A 50 year old headmaster was investigated for an 8 year history of recurrent absence attacks, stereotyped in nature and of sudden onset, each lasting about half a minute. He became pale, sweaty, and mentally withdrawn but did not fall down. Recovery was rapid and associated with transient headache. Previous neurological investigations, including repeated EEG and MRI, were negative. Electrocardiographic Holter monitoring disclosed only sinus bradycardia so he underwent head up tilt testing to exclude vasovagal syncope. Intra-arterial blood pressure and ECG were recorded continuously. Microneurography needles were positioned in the peroneal nerve of the right leg for recording efferent postganglionic MNSA.<sup>1</sup> This technique allows beat to beat monitoring and quantification of MNSA (bursts/min) which controls vascular tone in skeletal muscle. MNSA in turn is modulated by changes in blood pressure via the baroreflexes. Blood pressure

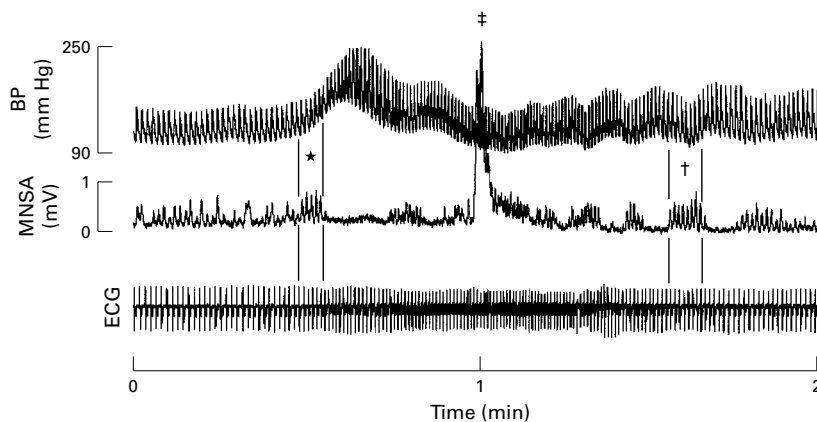


Figure 1 A 2 minute recording of blood pressure (BP), muscle nerve sympathetic activity (MNSA), and heart rate (ECG) during an absence attack after 10 minutes of head up tilt. At 30 seconds there was sudden mental withdrawal and a rapid increase in MNSA\* followed by a severe and paroxysmal increase in blood pressure and heart rate. As blood decreased, MNSA increased and when blood pressure normalised there was a marked baseline shift in MNSA†. During recovery, blood pressure and MNSA oscillated reciprocally (0.1 Hz)‡.

is normally maintained during head up tilt by increased MNSA and vasoconstriction.<sup>2</sup>

The patient showed normal blood pressure, heart rate, and MNSA responses to tilt initially, but after 10 minutes, he suddenly became pale, sweaty, and withdrawn for about 30 seconds. No loss of muscle tone was seen and he later confirmed that this was a typical absence attack. Coinciding with the onset of his symptoms, MNSA increased briefly for 3 seconds associated with a sudden increase in blood pressure from 138/95 to 222/150 mm Hg over 10 seconds. Heart rate simultaneously increased from 65 to 98 bpm (fig 1). Over the next 20 seconds, blood pressure and heart rate decreased and there was a major burst of MNSA followed by reciprocal oscillation of blood pressure with MNSA (0.1Hz) as blood pressure reached normal levels. During recovery, he complained of his usual transitory headache. Venous noradren-

aline (norepinephrine) concentrations were 1650 pmol/l and 5250 pmol/l before tilt and during recovery respectively. Normal values in our laboratory before and after 10 minutes of tilt are 456 (SD 50) and 705 (SD 74) pmol/l.<sup>3</sup> His absence symptoms could not be reproduced by rapidly increasing blood pressure to similar values (250/120 mm Hg for 30 seconds) with an intravenous bolus of epinephrine (100 µg). One week later, an EEG during a similar absence attack showed sharp waves arising from the left frontoparietal area (fig 2). Subsequent continuous EEG and blood pressure monitoring confirmed that focal seizure activity was simultaneous with paroxysmal hypertension. Studies with MRI showed hippocampal atrophy consistent with the diagnosis of complex partial seizure disorder. His absences were abolished with 400 mg carbamazepine daily and he has remained free of symptoms for 6 months.

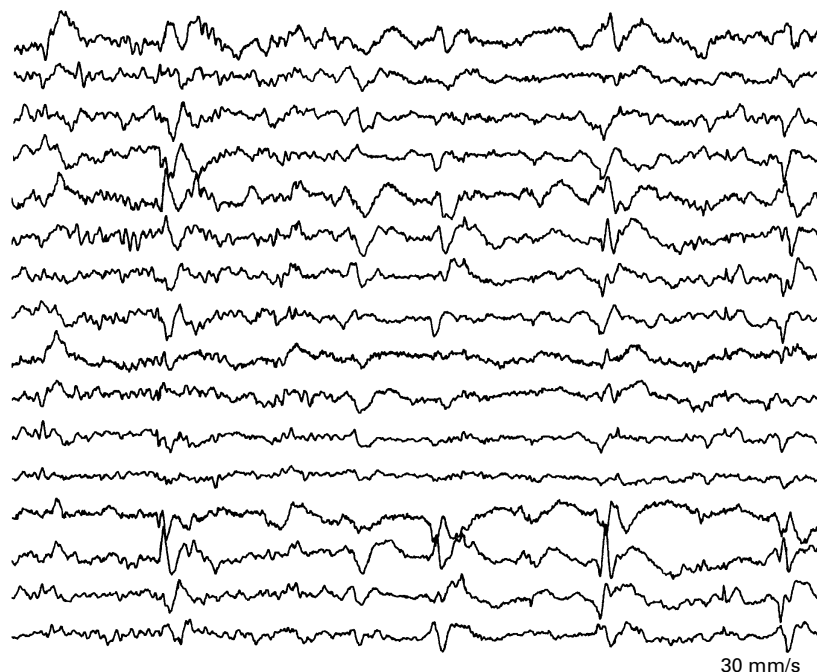


Figure 2 EEG recording obtained during light sleep showing sharp waves arising maximally in the left frontotemporal area. The montage consists of four sets of channels running anterior to posterior recorded from the right parasagittal, left parasagittal, right temporal, and left temporal areas respectively.

This is the first demonstration of paroxysmal neurogenic hypertension triggered by a seizure in a patient with complex partial seizure. The diagnosis of complex partial seizure was supported by the following: focal EEG changes during a subsequent absence seizure; no reproduction of absence symptoms during drug induced paroxysmal hypertension; characteristic hippocampal atrophy on MRI<sup>4</sup>; and complete response to anticonvulsant drugs. Other possible diagnoses including brain stem tumour, pheochromocytoma, and renal artery stenosis were excluded by appropriate imaging and neurohormonal analysis. Pseudoseizures were excluded on the basis of the EEG findings and the rapid response to treatment. Although rapid increases in MNSA and heart rate have been found during panic attacks, paroxysmal hypertension and loss of consciousness are not consistent features.<sup>5</sup>

The paroxysm consisted of simultaneous hypertension and tachycardia associated with sweating and facial pallor during the absence attack. We suggest that this is secondary to a generalised increase in sympathetic activity causing vasoconstriction and increased cardiac output. This is supported by (a) increased MNSA and heart rate despite progressive rise in blood pressure; (b) symptomatic blood pressure overshoot; (c) noradrenaline increased to over seven times the normal tilt levels; (d) prominent low frequency (0.1 Hz) oscillations in blood pressure and MNSA during recovery.<sup>2</sup> These low frequency oscillations (0.1 Hz) are thought to be secondary to changes in brain stem sympathetic activity separate from the effects of respiration, which are generally of a higher frequency (0.2 Hz). We emphasise that the initial increase in MNSA occurred when blood pressure was increasing and so was not baroreflex mediated as would be expected for respiratory or normal brain stem low frequency oscillations.

We hypothesise that this generalised increase in sympathetic activity is permitted by a transient interruption of baroreflex feedback inhibition during the seizure. We think that this is a unique recording of transient baroreflex failure characterised by a rapid and generalised increase in sympathetic activity, overriding the baroreflex afferents in the brain stem. It has long been suspected that paroxysmal hypertension occurs in complex partial seizures but to date, ambulatory monitoring has only demonstrated changes in heart rate.<sup>6</sup> Ambulatory beat to beat blood pressure monitoring would allow closer study of this phenomenon and its possible relation to sudden cardiac death in epileptic patients. Finally, this a good example of an episodic medical condition which may be very difficult to diagnose. Occasionally, when an episode is seen fortuitously in the laboratory, we may identify pathophysiology previously suspected but not actually seen.

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### Compression by looping and perforation of the facial nerve by the anterior inferior cerebellar artery: a possible cause of facial tic

Hemifacial spasm is a distressing, common, and well defined condition, which is difficult to treat. It is characterised by clonic and tonic contractions of the muscles supplied by the facial nerve, is intermittent, and is usually worsened by fatigue or emotional upsets.

A clinical picture similar to that of hemifacial spasm is also seen in trigeminal neuralgia, another condition for which widely varying pathophysiological bases, including vascular compression, have been proposed.<sup>1</sup>

In our case postmortem exploration of the posterior cranial fossa disclosed a strikingly abnormal relation between the anterior inferior cerebellar artery and VIIth cranial nerve. Such abnormal vascular anomalies around the facial nerve are repeatedly reported in the literature, and they seem to be closely correlated with hemifacial spasm.<sup>2</sup>

We took the cadaver of a man who had died aged 51, from the dissection material held by the First Department of Anatomy at the University of Vienna.

A square 2 cm×2 cm was drilled in the centre of the skull cap. formalin:water (1:5; 30 ml) was injected subdurally. The cadaver was left in the cold room for 24 hours. Then a mixture of phenol:formalin:water (3:1:10) was introduced into the femoral artery about 5 cm below the inguinal ligament through a 3 mm diameter cannula. Before preparation the cadaver remained in this phenol:formalin:water mixture for about 6 to 8 months.

The vascular anomaly reported was noted when the brain was moved carefully backwards. The brain, which was otherwise normal, was then dissected out of the cranial cavity. The external radius of the anterior inferior cerebellar artery was determined by a digital gauge.

During the exploration of the posterior cranial fossa of the cadaver, we encountered an unusual course of the right anterior inferior cerebellar artery (1.20 mm diameter), which arose from the lower third of the basilar artery and passed through the facial nerve 1.5 cm from the cerebellopontine angle, forming a ring around the nerve about 0.5 cm proximal to the point of penetration and compressing it at several points (fig 1).

The anterior inferior cerebellar artery first ran vertically downwards closely following the basilar and the right vertebral arteries. Then it took a horizontal course until it made a V shaped angle before penetrating the seventh cranial nerve. After it had passed through the facial nerve, with about one third of the fibres above it and two thirds below, its course made a ring around the seventh cranial nerve and disappeared between the cerebellum and the pons into the deep tissue. Along its course a branch went off to the choroid plexus of the fourth ventricle.

The cause and treatment of hemifacial spasm remain controversial. Whereas some theories postulate a cerebral or brain stem mechanism for its origin, others suggest that the causative lesion is within the facial nerve, either within the posterior fossa or at a more distal location.

Our unusual finding lends support to the neurovascular compression theory to explain the aetiology of this disorder as we would like to point out the unusual nature of this

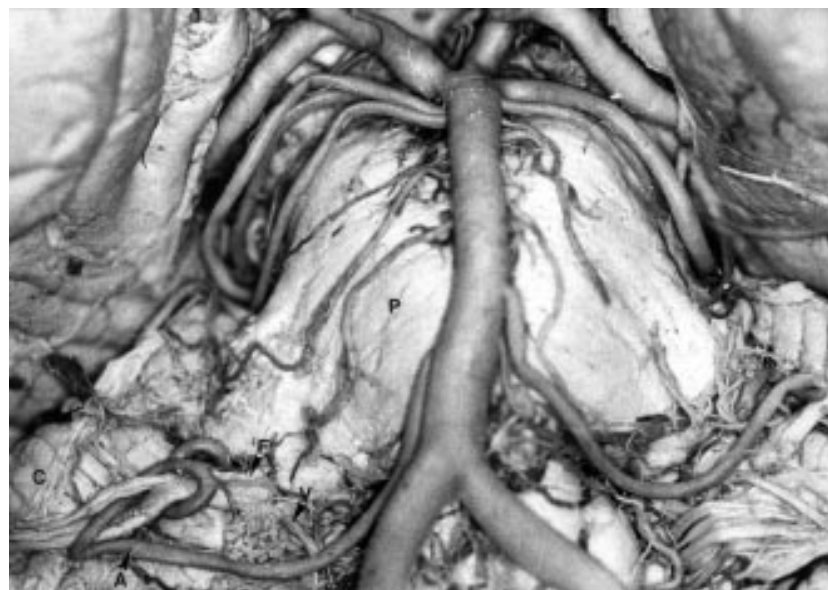


Figure 1 Inferior surface of the brain. A=Anterior inferior cerebellar artery; F=facial nerve (seventh cranial nerve); C=cerebellum; P=pons; V=vestibulocochlear nerve (eighth cranial nerve).

anatomical variety of the anterior inferior cerebellar artery.

During an investigation of the posterior cranial fossa, we became aware of an abnormal relation between a vessel and a nerve, which is not described in the current textbooks and encyclopedias. Although there is much literature reporting a close relation between the symptom "facial tic" and vessel variety<sup>3,4</sup>; our variety—that is, with both transfixion of the facial nerve and an arterial loop around the same nerve—has not been described in the specialist literature, nor has it been mentioned in the most recent review of variants.

Several authors have provided illustrations of a loop formed by the anterior inferior cerebellar artery, but without elaborating further on the topographic relation between the artery and the internal acoustic meatus or the seventh and eighth cranial nerves. It has been asserted that this vessel seldom appears on radiographs.

Typical hemifacial spasm is caused by vessels on the antero-caudal side of the nerve, whereas atypical hemifacial spasm is caused by vessels on the posterior rostral side.<sup>5</sup>

The relevant aspect of this article lies in its emphasis on the connection between the neurological symptoms and this anatomical variety of a nerve.

The deceased had begun to experience intermittent symptoms of varying intensity in his face at the age of 49. These symptoms took the form of uncontrollable twitching at the right corner of his mouth, ipsilateral hearing impairment, retroauricular cramps, and retroauricular sensory impairment. According to the case history, the deceased had undergone a full otorhinolaryngological examination and pure tone speech audiometry during his lifetime. Thus, it was possible to diagnose the perceptive unilateral acoustic hypoacusia on the right. Early auditory evoked potential studies had also been performed showing an increase in latency and a decrease in amplitude without any deterioration of morphology of the waves. It had not been possible to use MR for the diagnosis as he had a pacemaker in place. None of these symptoms responded to therapy with botulinum toxin.

In our case the compression of the facial nerve at several points could have led to irritation of the region supplied by the posterior auricular nerve and in this way to the symptoms described above.

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## CORRESPONDENCE

### Charles Bonnet syndrome: an example of cortical dissociation syndrome affecting vision?

This letter is a response to that by Abhijit Chaudhuri.<sup>1</sup> I thank Chaudhuri for his kind comments, but will address his surprise that I did not comment on the Charles Bonnet syndrome in my 1999 paper.<sup>2</sup>

Chaudhuri and his associates cannot be really criticised for using the eponym "Charles Bonnet syndrome" for the "triad of visual hallucinations, visual sensory deprivation, and preserved cognitive status" as there is support in the literature for the use of the eponym in this way. But I favour the use of the eponym, if it is to be used at all, only in patients with eye disease. This was what Charles Bonnet described,<sup>3</sup> and the way the term was initially used by de Morsier in 1936.<sup>4</sup> I highly recommend the paper by flytche and Howard<sup>5</sup> in which the authors provide an excellent summary of Charles Bonnet syndrome on pages 1253-1254. I agree with the way that they accept the use of the term, and their reason for doing so. It is, thus, a matter of personal opinion as to how the eponym should be used. It was never used in any of the references in my 1999 paper, but I did not choose the references with this reason in mind.

Is there any reason to use the eponym at all? It may remind ophthalmologists that visual hallucinations can occur with ocular disease and do not necessarily suggest a neurological lesion. But, as the eponym has now acquired two different meanings I think that it leads to more confusion than clarification. Chaudhuri's communication is a good example. I would thus suggest that it no longer be used. I did not use the term because I did not, and do not, think that the subject of my report (myself) has the Charles Bonnet syndrome. Nor, presumably, did the reviewers of my paper and the Editor of this *Journal*.

Finally, I must tell Chaudhuri that "advanced age" hardly begins at 60 years.

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### Effects of topiramate on cognition

This letter concerns the recently published study by Thompson *et al*,<sup>1</sup> reporting the authors' findings on cognitive effects with topiramate. Firstly, I want to correct the authors' mischaracterisation of a review paper of mine. The authors state that "the literature on antiepileptic drugs ... emphasised positive psychotropic effects," referencing only a 1998 review in which I discussed cognitive and psychotropic effects of antiepileptic drugs. Although I mention some positive effects, I also discussed negative effects, including studies from my own centre that have shown significant negative psychotropic and cognitive drug effects.

Secondly, I provide some perspective on the report of Thompson *et al* of clinically significant cognitive declines in 18 patients treated with topiramate as adjunctive therapy. The authors correctly conclude that "caution is warranted in the interpretation of the findings due to methodological limitations of the study design." Because their study was retrospective and observational, it is susceptible to considerable subject selection bias. For example, five of the 18 patients were specifically included in the topiramate sample because they reported cognitive effects.

The only way to minimise effects that may bias study conclusions is to conduct a prospective randomised controlled study. Two such studies have recently compared topiramate and valproate as add on therapy to carbamazepine, using comprehensive neuropsychological batteries to objectively measure drug effects.

At the end of 3 months of maintenance therapy, only one of 17 (6%) variables in one study<sup>2</sup> and only two of 30 variables (7%) in the other<sup>3</sup> were significantly worse for topiramate compared with valproate. For the three variables with statistically significant differences, the mean differences in change scores were modest. Analysis of individual data showed that scores were unchanged or even improved in most patients receiving topiramate and valproate. Statistically significant differences could be accounted for by a minority of patients receiving topiramate in whom scores deteriorated >1 SD from baseline. I suggest that the patients reported by Thompson *et al* likely represent a similar subgroup of patients.

Physicians should be aware that a subgroup of patients treated with topiramate may experience clinically significant cognitive effects. When these effects occur, they are generally apparent to the patient or family members and can therefore be monitored with routine clinical evaluations. Alternatively, a brief cognitive test (for example, a verbal fluency test or symbol digit modalities test) should easily detect changes of the magnitude reported. In a subgroup of patients, topiramate may need to be discontinued if cognitive effects do not resolve over time with slowed titration or dosage reduction.

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# The authors reply:

We write in response to the letter of Meador. We concur that his review article discusses both positive and negative psychotropic effects of antiepileptic medication.

Meador comments on the biased nature of our patient sample. However, we think that we adequately emphasised that our study was not randomised or controlled but carried out in a clinical environment. We pointed out that some of the patients had been referred due to cognitive complaints. Furthermore we acknowledged studies which reported no cognitive effects of the drug including the valproate and topiramate study and drew attention to the conflicting findings. We agree that prospective randomised controlled trials are the way to minimise selection bias. However, they are not the be all and end all. Bone marrow aplasia with felbamate and visual field constriction with vigabatrin treatment were not found in randomised controlled trials but by the careful clinical study of patients. This is an analogous situation. Randomised controlled trials are not without their own biases as most will be sponsored by the pharmaceutical industry and it would be naïve to conclude that this does not influence the presentation of the results.

We agree with Meador that the adverse effects of topiramate reported are likely to occur in a minority of patients treated with the drug. However, we think that this may represent a clinically significant number of patients, particularly in those attending tertiary referral centres. Negative effects, however small the numbers, are worthy of reporting and of further exploration. The question our findings raise is not does topiramate have adverse effects but rather why does it have adverse effects in some people?

We agree with Meador's final point and indeed this was one of the intended take home messages of our paper. This is why we chose to submit to a journal with a broad readership who would have much less experience with topiramate. We hoped that our paper would draw attention to a group of patients who should be prioritised for neuropsychological monitoring and highlight the type of measures that could be employed showing that an extensive assessment is not necessary.

We, however, do not think that the cognitive changes experienced would be obviously attributed to topiramate treatment. Most patients in the study were not referred because of cognitive complaints. Six were being seen as part of their presurgical assessment and indeed were not considered good candidates due to their neuropsychological test profiles. For some the cognitive complaints did not occur in association with the introduction of topiramate or with any change in dosage and did not seem to develop until they had been on the drug for several months. For such patients, particularly those with left hemispheric pathology, increases in word finding problems and other

verbal difficulties are more likely to be attributed to the underlying pathology and ongoing seizures than to a drug effect. Topiramate is a useful antiepileptic drug but it may lead to adverse cognitive changes and we need to be alert to this.

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## Postoperative hearing loss due to venous congestion at the inferior colliculus, or cochlear dysfunction?

I read with interest the article by Strauss *et al* on postoperative contralateral hearing loss which developed on the third day after microvascular decompression for trigeminal neuralgia. They attributed the symptoms to venous congestion at the ipsilateral inferior colliculus after dissection of the pontotrigeminal vein, which was documented by MRI. Symptoms resolved partially after intravenous rheologic medication for a total of 19 days. The authors' explanation for the delayed postoperative hypacusis, however, merits further discussion. Strauss *et al* provided preoperative and postoperative recordings of brain stem auditory evoked potentials: postoperatively, after stimulation on the operated side, ipsilateral waves I through V, and contralateral waves II through V are all clearly identifiable, contrasting with stimulation on the non-operated side, depicting only a small wave V bilaterally, but no other components. This pattern suggests a left sided lesion involving the generator of wave I—presumably the auditory nerve near the cochlea—and is also consistent with the patient's pancochlear hearing loss.<sup>2-4</sup> By contrast, brain stem lesions—unless damaging the cochlear nucleus—are usually not associated with pure tone hearing loss, but rather with abnormal auditory localisation or interaural time discrimination,<sup>2,5</sup> as auditory impulses are conveyed bilaterally in the brain stem.<sup>2-4,6</sup> Furthermore, a brain stem lesion causing profound hearing loss is likely to produce also contralateral wave IV/V abnormalities after stimulation on the non-affected side, but even the severest brain stem lesions, such as in evolving brain death, do not affect wave I.<sup>1</sup> The vascular supply of the mesencephalic brain stem differs from that of the inner ear, the first being fed by mesencephalic arteries via the posterior cerebral or superior cerebellar artery, and drained through the superior petrosal vein; the second being supplied by the more caudally originating labyrinthine artery via anterior—or occasionally posterior—inferior cerebellar artery, and drained by the labyrinthine vein through the posterior part of the superior petrosal or transverse sinus, and the internal jugular vein.<sup>6</sup> Although the patient's hearing may have been partially affected by the documented mesencephalic lesion, hearing loss may in fact be more likely caused by concomitant cochlear dysfunction. An ischaemic lesion seems probable, presumably postoperative vasospasm, or—less likely—unrelated embolism. In either situation, rheologic treatment may have been benefi-

cial, as well as in venous congestion of the inferior colliculus. Concomitant cochlear dysfunction should have been considered as a cause of hearing loss in this patient, or ruled out by further examination.

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## Strauss replies:

We appreciate Kofler's comment on our paper and his interest in this unusual and still poorly understood clinical picture. We agree that the brain stem auditory potentials (BAEPs) after contralateral stimulation do not clearly point to a lesion of the ipsilateral colliculus; however, to our knowledge the neurophysiology of auditory pathways within the brain stem is not yet fully understood. For example, in our series of more than 300 cases of acoustic neuroma monitoring we have made the observation that the contralateral wave V is much more pronounced compared with the ipsilateral wave V. The advantage of this case report is the preoperative and postoperative radiological and clinical documentation. The delayed onset of symptoms several days after the surgical procedure, the lack of effect of calcium blocker therapy—actually the patient's pure tone audiogram and speech discrimination deteriorated under nimodipine treatment—and the hearing improvement after heparinisation do not suggest vasospasm as the underlying pathophysiological mechanism. The literature on this rare yet important phenomenon of contralateral hearing loss after cerebellopontine angle surgery is purely speculative. By contrast this case report follows a straight course, which started at surgery with dissection of the pontotrigeminal vein, followed by a delayed contralateral hearing loss, and ended with a lesion of the ipsilateral colliculus. This lesion was not documented on preoperative MRI. Taking these findings into consideration, together with the neurophysiological findings of BAEPs in a still not fully understood auditory pathway within the brain stem, the "isolated vasospasm theory" seems unlikely.

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## BOOK REVIEWS

**Behaviour and mood disorders in focal brain lesions.** Edited by JULIEN BOGOUSLAVSKY and JEFFREY L. CUMMINGS. (Pp554, £49.95). Published by Cambridge University Press, Cambridge, 2000. ISBN 0-521-77482-9.

This book has arisen because of the comparative dearth of studies examining the emotional and behavioural consequences of focal brain lesions and, if nothing else provides a useful compendium of this literature in 18 chapters written by experts in the field. The first three chapters set the scene by providing a conceptual overview and discussions of methodological issues. The rest are devoted to specific topics and generally take the form of either examinations of the evidence for the localisation of specific neuropsychiatric syndromes (depression, mania, obsessive compulsive disorder, psychosis) or reviews of the effects of lesions of particular structures (thalamus, basal ganglia, frontal lobe, temporal lobe). In their overview, Cummings and Bogousslavsky group the disorders of mood, thought, affect, and motivation considered in this book under the rubric "fundamental dysfunctions" which they point out are associated with interruptions of limbic and frontosubcortical circuitry. This diffuse nature of these circuits is reflected in the finding that lesions of disparate areas can produce, for example, psychotic phenomena and that lesions in specific structures—for example, thalamus or basal ganglia, can result in a range of behavioural and emotional abnormalities. It is thus often difficult to make strong inferences from this literature about the neural basis of emotion and behaviour. Indeed some chapters are essentially categorised lists of studies without much in the way of theoretical underpinning. Several chapters, by Habib (disorders of motivation), Eslinger and Geder (behavioural and emotional changes after focal frontal damage) and Tranel (neural correlates of violent behaviour), stand out. These stray from localisation and bring in evidence from basic neuroscience and human functional neuroimaging to inform and interpret fascinating case histories in terms of a functional neuroanatomy of emotion and behaviour.

EILEEN JOYCE

**Update in neurology for general practitioners.** By P. ORTON, D. BATEMAN, G. FULLER, P. NEWMAN, D. PARK, R. SHAKIR, and G. YOUNG. (Pp 218 + 2 CD—ROM, £80.00) Published by University of Bath/British and Spine Foundation/Royal College of General Practitioners, Bath, 2000.

The seven authors of this text are to be congratulated on their innovative approach and the freshness they bring to the evaluation of the common neurological problems encountered in primary care. This text and the two accompanying CD ROMs represent a cooperative venture between the British Brain and Spine Foundation, the Royal College of General Practitioners and the University of Bath.

The text addresses the commonly encountered problems of headache, sensory disturbance, cerebrovascular disease, dementia, confusion, movement disorders, fits and faints, and back, leg, and arm pain. The approach is a simple one—namely, a definition of the condition or conditions, who gets it? What causes it? How does it present? What is the differential diagnosis? How is it investigated and managed? This pragmatic approach pays special attention to the prevalence of each disorder in the community and contains "red flags" where there is diagnostic doubt and uncertainty. The two accompanying CD ROMs outline learning outcomes, case histories, self assessment questionnaires, and case pathways with respect to investigation, management, and prognosis. Each such case is linked with the text providing assignments in clinical audit, comment, documentation of data, and "setting standards". Incorporated in all of this are useful components such as data collection sheets for specific symptoms and summary sheets to aid and improve documentation.

I found this an interesting book and enjoyed finding my way around the CDs, which were easy to use. I would imagine that this would be a valuable aid for the busy general practitioner and should help set standards in primary care that would aid patients and ensure thorough evaluation before referral. The only thing missing was guidance demarcating between evaluation in the primary care setting from the need to refer on for a specialist opinion. All of us occasionally think, under moments of work overload, that our colleagues in primary care could be a little more circumspect in whom they refer (although the truth of the matter is that most referrals are thoughtful and necessary). A text such as this with no obvious competitor, is long overdue, written by neurologists who, along with their general practitioner colleague, have adopted a common sense approach to their task. I would strongly recommend this book with its accompanying CD ROMs to my general practitioner colleagues in the belief that it would serve to demystify our specialty. Perhaps in future editions the authors might consider incorporating referral guidelines that would be a useful supplement to a text that, for example, takes general practitioners through from the suspicion of brain tumour to the process of biopsy and subsequent radiotherapy. While such data informs and allows the practitioner to explain to his or her patient what they might expect to encounter in the process of investigation and treatment, it does not clearly define who does what and when.

In conclusion, I recommend this innovative text, which, although directed primarily at our general practitioner colleagues, contains something for all on the simple approaches of evaluation, the importance of documentation, and the value of using an interactive CD ROM as an educational tool. I think that this text goes a long way not just to educate and entertain, but also remove from primary care, the notion that neurology is a difficult and uncertain area.

IAN BONE

**Rehabilitation of visual disorders after brain injury.** By J. ZIHL (Pp 187, £29.95). Published by Psychology Press, Hove, 2000. ISBN 0 86377 898 4.

This is the second series on neuropsychological rehabilitation fostered by Barbara Wilson and Ian Robertson (the first being *Neural repair, transplantation, and rehabilitation* by R. Barker and S. Dunnett). The renewed interest is welcome. Josef Zihl is one of the first clinical scientists, together with collaborators such as von Cramon, to have put a concentrated effort into rehabilitation of visual disorders, spanning a period of 2 decades. Much of this pioneering work lies in Germany, stemming from an older tradition going back to Poppelreuter, and the current book should make the developments better known outside that country. It remains something of a curiosity that visual rehabilitation is scarcely pursued in Britain and the United States, especially given the seminal animal work (by Cowey in Britain and Mohler and Wurtz in the United States) clearly demonstrating the potential capacity for recovery after V1 lesions in the monkey, with practice regimes. Indeed, Zihl's own work acknowledges the influence of these animal studies on his own research.

The Series preface describes this work as a "modular handbook". Handbook it is not. Rather it is a compact and relatively short account that is more like a progress report, full of interesting approaches described in mid-stream of the research, much of it still to be completed. It is broad ranging, the largest and most advanced section (about half of the book) being on visual field disorders, but progressing to visual acuity, colour vision, visual space perception (including Balint's syndrome), visual agnosia, and a final brief section on the special problems of a central scotoma. Each section starts usefully with evidence of spontaneous recovery, which is the baseline from which rehabilitative efforts must be assessed. Such efforts are almost entirely based on intensive practice (what I have called "grindsight"). Zihl is very cautious, lacing the evidence with statements such as "our observations produce preliminary evidence that spatial contrast sensitivity can, in principle, be improved by specific and systematic practice. However, the limited number of cases does not allow definite conclusions to be drawn .....". (p 96). He is also careful to distinguish between measurable effects in the laboratory and their "ecological value" to the subject in terms of any benefit in everyday life. In some regards he is over-cautious—for example, in his speculation (with von Cramon) "that recovery of visual field defects can only be expected with complete striate cortex injury" (p 34). Of course, complete V1 lesions are almost always accompanied by additional damage, when animal work demonstrates a reduced residual capacity. But a complete but restricted V1 removal in the monkey still allows further recovery to take place.

Anyone wishing to find practical approaches for helping patients across a range of visual disorders will find this a useful, humane, and dedicated book. He or she will have to work through a compact monograph and share Zihl's experience with him, rather than find a collection of shorthand recipes. It will be rewarding work.

L. WEISKRANTZ

**An odd kind of fame. Stories of Phineas Gage.** Edited by MALCOLM MACMILLAN (Pp 552, £24.95). Published by Massachusetts Institute of Technology, USA, 2000. ISBN 0 262 13363 6.

A brief description of the contents of this book, which is 562 pages long and deals purely with the case of Phineas Gage, would lead most potential readers to throw up their hands in horror and to assume that the book must be extremely repetitive and boring. Nothing could be further from the truth. Malcolm Macmillan's approach in this book has similarities to James Joyce's concept when writing *Ulysses*. Joyce thought that all of life's experiences could be encapsulated in the description of 1 day in the life of his Dublin characters. Malcolm Macmillan's unstated thesis is clearly similar and that a great deal of 20th century cognitive neuroscience can be understood by the analysis of the remarkable case of Phineas Gage.

This book is the outcome of an obsession with Phineas Gage which must have extended over many years. It is superbly written and provides a fantastic reference source across a wide range of topics. The first few chapters describe, in detail, the events surrounding the fateful afternoon of 13 September 1848 when the unfortunate Phineas Gage was tamping an explosive charge close to Cavendish in Vermont. The tamping iron was propelled through Phineas' skull damaging his orbit and presumably destroying much of the orbitofrontal cortex. The iron landed 20 metres away and can be seen in the Anatomical Museum at Harvard University. There are many revelations in this part of the book. It was certainly not known to me that the original interest in Harlow's description of Phineas Gage revolved around the surgical procedures Harlow carried out which saved Gage's life. It was only 20 years later, in 1868, that Harlow described (very briefly) the changes in personality that have become enshrined in neurological and neuropsychiatric folklore.

The second section of the book is in many ways the most fascinating. Malcolm Macmillan provides a scholarly account of the origins of the concept of cognitive localisation in the brain outlining the contributions of Laycock, Hughlings Jackson, Ferrier, Gall, and Broca. There is also a chapter on the contribution, or otherwise, of Gage's story to the origins of psychosurgery. Macmillan has unearthed a great deal of overlooked early literature on the use of various procedures used for the surgical treatment of insanity in the late 19th and early 20th centuries. I was particularly fascinated by the sections describing the effects of frontal lobe resection and ablation.

The following section of the book deals with interpretations of the changes in Gage's personality and its contribution to both the scientific and popular literature. The final chapter details the life of Dr John Martin Harlow. The main text is followed by facsimiles of the Gage papers. There are also reproductions of the CT of Phineas Gage's skull.

I can thoroughly recommend this book to anyone interested in the history of neuroscience, neuropsychology, or neuropsychiatry. It is also amazing value at just under £25.

JOHN HODGES

**Management of headache and headache medications, 2nd edition.** By LAWRENCE D ROBBINS (Pp 296, US\$49.00). Published by Springer-Verlag, New York, 2000. ISBN 0-387-98944-7.

Dr Lawrence Robbins, from Rush Medical College, Chicago has revised his deservedly popular 1994 text on the management of

idiopathic headache syndromes. He shares a wealth of clinical experience in the drug therapy of difficult headache patients, with necessarily brief descriptions of clinical features and pathogenesis. Although there is an extensive list of references at the end of the book, they are not cited directly in the text, and the book reads as one man's recipe book rather than a systematic review of published trials, or of the pharmacological or clinical evidence supporting management decisions. It is inevitable that the range of drugs recommended is American, with more emphasis on narcotic and barbiturate combinations and no mention of domperidone or pizotifen, but there is a useful glossary of United States trade names as an appendix.

The chapters on the acute and preventative management of migraine, tension headache, and cluster headache are followed by illustrative case histories, from which it is soon apparent that the tendency of United States patients to see many neurologists and complain more about side effects can lead to the use of an extremely wide range of drugs, sometimes making one's own multiple efforts on behalf of a challenging tertiary referral seem straightforward by comparison. There is a particularly useful chapter on headache in patients aged over 50, post-traumatic headache, lumbar puncture headache, chronic paroxysmal hemicrania, and SUNCT.

Although filled with much clinical wisdom from a vastly experienced author, the book has the feel of a catalogue; for European readers it is more likely to have a role as a desktop reference text.

RICHARD PEATFIELD

**Vascular dementia.** Edited by JOHN STIRLING MEYER *et al* (Pp 320, US\$88.00). Published by Futura Publishing, Armonk, 2001. ISBN 0 87993 425 5.

This is a short text of 306 pages in 17 chapters covering vascular dementia.

Although it is a multiauthor text, there are only 11 authors so many of the chapters have authors in common. The principal editor, Dr Meyer, coauthors no less than 10 of the 17 chapters. As a result of this many authorities are not included among the list of contributors and some of the chapters are not fully authoritative.

The text gives a fairly good overview of the subject, although there are some unusually prominent inclusions including full chapters on plasmapheresis and estrogen replacement therapy in the treatment of vascular dementia, neither of which are recognised treatments. Some of the more important recently recognised conceptual issues, including the very high preponderance of mixed dementia (vascular dementia and Alzheimer's disease) and the issue of diagnosis before reaching the state of being demented are scarcely covered at all. The limitations of the current formal diagnostic criteria for vascular dementia are touched on, but not considered in detail and the chapter on diagnosis really does not help in this respect.

Overall, this book provides an adequate background to the subject but a person interested in the topic would need to look elsewhere for some of the more recent critical issues.

JOHN BOWLER

**Headache in primary care.** By SD SILBERSTEIN, RB LIPTON, PJ GOADSBY, and RT SMITH (Pp 192, £29.95). Published by Isis Medical Media, Oxford, 1999. ISBN 1-901865-66-5.

A wide range of textbooks are now available on the topic of headache, ranging from short notes of 40 or 50 pages up to encyclopaedic tomes. This book falls into the middle of the range, being an easy read of 165 pages.

The work is divided into three broad categories: (1) pathophysiology and epidemiology of headache, (2) primary headache disorders, and (3) secondary headache disorders.

In the first section, the starting point is the International Headache Society (IHS) classification but the bridge to the clinical approach to patients is rapid and the use of disability assessment tools is discussed. The epidemiology of the various forms of headache is then examined, together with impact on the sufferer. An entire chapter is devoted to diagnostic testing, particularly to exclude ominous causes of headache, and finally the pathophysiology of primary headache is discussed, the focus being on migraine. Genetics, anatomy, and physiology are all investigated. This whole section is concise and informative, giving a very good overview of the subject.

The rest of the book is divided into chapters dealing with specific types of headache, the first section looking at migraine, tension-type headache, chronic daily headache, cluster headache, and related symptoms, the final section covering secondary headache, including post-traumatic headache, headache associated with disease of the intracranial cavity, sinus headache, headache associated with CNS infection, headache associated with pregnancy and breast feeding, and geriatric headache. Within these chapters, all types of presentation and management are discussed, the emphasis being on the use and application of the IHS classification in a clinical setting.

This book undoubtedly contains the full range of information necessary to deal with the treatment of headache. However, the clinical chapters are written from a predominantly American perspective and, therefore, the therapeutic approaches in particular do not necessarily correlate with those used in the United Kingdom. Because of the comprehensive nature of the work, there is a danger that the reader may not appreciate the relative importance of some of the various conditions discussed. For instance, my own experience has shown that the greatest clinic problem, even in a primary care setting, comprises patients with chronic daily headache and analgesic dependence. Important basic clinical issues such as this may be lost within the wealth of information set out here.

My overall impression is that this is a very comprehensive book which would serve as a good reference. However, although it would be extremely useful for the primary care doctor in the United States where more specialisation exists, its value in the United Kingdom may be limited to the secondary care doctor or to the few primary care doctors who have a specific interest in headache.

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